EXPRESS MAIL LABEL NO. EV352377100US
Date of Deposit: December 27, 2004
Attorney Reference Number 4239-66176-05

Claims

1. (currently amended) A ~~variant~~ humanized CC49 antibody, comprising:

a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3,

wherein a L-CDR3 of the ~~variant~~ humanized CC49 antibody or of a functional fragment of the ~~variant~~ humanized CC49 antibody comprises a non-conservative amino acid substitution, and wherein the ~~variant~~ humanized CC49 antibody has a high binding affinity for TAG-72, compared to a parent CC49 antibody.

2. (currently amended) The ~~variant~~ antibody of claim 1, wherein the non-conservative substitution is a tyrosine to proline substitution.

3. (currently amended) The ~~variant~~ antibody of claim 1, wherein the non-conservative substitution is at position 91.

4. (currently amended) The ~~variant~~ antibody of claim 1, wherein the non-conservative substitution is at a position that corresponds to a ligand contact residue.

5. (canceled)

6. (currently amended) The ~~variant~~ antibody of claim 1, wherein the L-CDR1 and L-CDR2 are a human antibody L-CDR1 and L-CDR2, respectively.

7. (canceled)

8. (currently amended) The ~~variant~~ antibody of claim 1, wherein the high binding affinity is at least about 1.2×10^{-8} M.

9. (canceled)

10. (currently amended) The ~~variant~~ antibody of claim 1, wherein the antibody is minimally immunogenic.

11. (currently amended) The ~~variant~~ antibody of claim 1, wherein the antibody further comprises an effector molecule.

12. (currently amended) The ~~variant~~ antibody of claim 11, wherein the effector molecule is a detectable label.

13–15. (canceled)

16. (currently amended) The ~~variant~~ antibody of claim 1, further comprising at least one additional non-conservative amino acid substitution in the L-CDR1.

17–19. (canceled)

20. (original) A humanized CC49 antibody, wherein a nucleic acid sequence encoding the antibody has an ATCC Accession number comprising ATCC Accession number PTA-4182 or ATCC Accession number PTA-4183.

21. (currently amended) A nucleic acid molecule encoding the ~~variant~~ humanized monoclonal antibody of claim 1.

22. (original) A vector comprising the nucleic acid of claim 21.

23. (currently amended) A ~~variant~~ humanized CC49 antibody, comprising:

a variable light framework region and a variable heavy framework region of a human antibody;

a light chain complementarity determining region (L-CDR)1, a L-CDR2, a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-

CDR3, wherein at least one complementarity determining region (CDR) is a human antibody CDR and remaining CDRs are murine CC49 antibody CDRs;

a non-conservative substitution of a first residue, wherein the first residue is in the L-CDR3 of the ~~variant~~ antibody; and

a substitution of a second residue, wherein the second residue is in a any L-CDR or H-CDR of the ~~variant~~ antibody;

wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody.

24. (currently amended) The ~~variant~~ antibody of claim 23, wherein the non-conservative substitution of the first residue is a tyrosine to proline substitution.

25. (currently amended) The ~~variant~~ antibody of claim 23, wherein the non-conservative substitution of the first residue is at position 91.

26. (currently amended) The ~~variant~~ antibody of claim 25, wherein the non-conservative substitution of the first residue at position 91 is a tyrosine to proline substitution.

27. (currently amended) The ~~variant~~ antibody of claim 23, wherein the antibody further comprises an effector molecule.

28. (currently amended) The ~~variant~~ antibody of claim 27, wherein the effector molecule is a detectable label.

29–31. (canceled)

32. (currently amended) A method of detecting a TAG-72-expressing tumor in a subject, comprising:

contacting a sample ~~obtained~~ from the subject *in vivo* or *in vitro* with the ~~variant~~ antibody of claim 1 for a sufficient amount of time to form an immune complex; and

detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.

33. (original) The method of claim 32, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

34. (currently amended) The method of claim 32, wherein the ~~variant~~ antibody further comprises an effector molecule.

35. (currently amended) The method of claim 34, wherein the effector molecule is a detectable label or a toxin.

36-43. (canceled)

44. (currently amended) A method of treating a subject having a tumor that expresses TAG-72, comprising administering to the subject a therapeutically effective amount of the ~~variant~~ antibody of claim 1, wherein administering the therapeutically effective amount of the ~~variant~~ antibody of claim 1 inhibits the growth of the tumor or reduces the size of the tumor, thereby treating the subject.

45. (currently amended) The method of claim 44, wherein the administration of a therapeutically effective amount of the ~~variant~~ antibody of claim 1 does not elicit a human anti-murine antibody response in a subject.

46. (canceled)

47. (currently amended) The method of claim 44, wherein the ~~variant~~ antibody further comprises an effector molecule.

48. (currently amended) The method of claim 47, wherein the effector molecule is a toxin or a radioactive isotope.

49–51. (canceled)

52. (currently amended) A pharmaceutical composition comprising a therapeutically effective amount of the ~~variant~~ antibody of claim 1 in a pharmaceutically acceptable carrier.

53–55. (canceled)

56. (currently amended) The ~~variant~~ antibody of claim 1, wherein the parent ~~humanized~~ CC49 antibody is HuCC49V10.

57-66. (canceled)

67. (currently amended) The ~~variant~~ antibody of claim 23, wherein the non-conservative substitution of the first residue at position 91 is a tyrosine to proline substitution, the substitution of the second residue at position 27b is a valine to leucine substitution, the L-CDR1, L-CDR2, L-CDR3, H-CDR1, H-CDR2, and H-CDR3 are the parent CC49 antibody L-CDR1, L-CDR2, L-CDR3, H-CDR1, H-CDR2, and H-CDR3, respectively, and the parent CC49 antibody is HuCC49V10.